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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,819	01/17/2001	Christopher J. Stanley	PM 275510 P5642US	5588

25225 7590 07/01/2004

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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/760,819	STANLEY, CHRISTOPHER J.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,13,18 and 21-23* is/are rejected.

7)☒ Claim(s) *7-12,14-17,19 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 January 2001 (original)* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/313,385* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission of RCE filed on May 10, 2004 and the amendment filed on March 8, 2004 have been entered. The claims pending in this application are claims 1 and 3-23. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of amendment filed on March 8, 2004.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claim 13 recites the limitation "said second primer" in the claim. There is insufficient antecedent basis for this limitation in the claim since there is no second primer in claims 1, 7, and 8. Please clarify.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Walker (US Patent NO. 5,455,166, published on October 3, 1995).

Walker teaches strand displacement amplification.

Regarding claim 1, Walker teaches a method of amplification of a target nucleic acid sequence (and its complementary strand) in a sample by endonuclease mediated strand displacement. The method involves the steps of: 1) isolating nucleic acids suspected of containing the target sequence from a sample, 2) generating single stranded fragments of target sequences, 3) adding a mixture comprising (a) a nucleic acid polymerase, (b) deoxynucleosidetriphosphates including at least one substituted deoxynucleosidetriphosphate and (c) at least one primer which is complementary to a region at the 3' end of a target fragment and further wherein each primer has a sequence at the 5' end which is a recognition sequence for a restriction endonuclease, and 4) allowing the mixture to react for a time sufficient to generate reaction products (see column 4, last paragraph and column 5, first paragraph). Since Walker teaches adding a mixture comprising a nucleic acid polymerase, deoxynucleosidetriphosphates and at least one primer which is complementary to a region at the 3' end of a target fragment,

and allowing the mixture to react for a time sufficient to generate reaction products (see column 4, last paragraph and column 5, first paragraph) wherein the at least primer is labeled with alkaline phosphatase (see column 4, third paragraph), and it is known that alkaline phosphatase has a molecular weight in excess of 80,000 Daltons, links to a nucleic acid via a covalent bond (see previous office mailed on January 7, 2004) and is water soluble (see attachment for alkaline phosphatase), Walker disclose providing a primer being bonded to a carrier macromolecule having a molecular weight in excess of 80,000 Daltons (ie., the primer labeled with alkaline phosphate conjugate taught by Walker), hybridizing the bound primer to said template (ie., a target fragment taught by Walker); and extending said primer to form an extended primer (ie., reaction products taught by Walker) which replicates from said template wherein said carrier macromolecule is water soluble at a temperature in the range of 0-60°C as recited in claim 1.

Therefore, Walker teaches all limitations recited in claim 1.

7. Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Bronstein (US Patent No. 5,220,005, published on June 15, 1993).

Regarding claim 18, Bronstein teaches to hybridize a DNA probe labeled with alkaline phosphatase with nucleic acids immobilized on a nitrocellulose membrane and detect the hybridization (see column 13, lines 44-61). Since alkaline phosphatase is directly and covalently attached to the DNA probe and it is known that alkaline phosphatase has a molecular weight in excess of 80,000 Daltons, the DNA probe taught by Bronstein is a first nucleic acid bound to a non-nucleotide carrier macromolecule having a molecular weight in excess of 80,000 Daltons (ie., alkaline phosphatase) as recited in the claim. Since it is known that cellulose is a complex

carbohydrate, or polysaccharide consisting of 3,000 or more glucose units and glucose has a formula of ($C_6H_{12}O_6$) with a molecular weight of 180.2 Daltons (see an attachment for cellulose in previous office action mailed on January 7, 2004), a nucleic acid that is complementary with the DNA probe and is immobilized on a nitrocellulose membrane is a second nucleic acid bound to a non-nucleotide carrier macromolecule having a molecular weight in excess of 80,000 Daltons as recited in the claim. Since Bronstein teaches to hybridize a DNA probe labeled with alkaline phosphatase with nucleic acids immobilized on a nitrocellulose membrane and detect the hybridization (see column 13, lines 44-61), Bronstein discloses contacting said first and second nucleic acids under hybridization conditions and detecting hybridization between said first and second nucleic acids as recited in the claim.

Therefore, Bronstein teaches all limitations recited in claim 18.

8. Claims 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Van Ness *et al.*, (US Patent NO. 5,667,976, priority date: May 11, 1990).

Van Ness *et al.*, teach Solid supports for nucleic acid hybridization assays.

Regarding claim 21, since Van Ness *et al.*, teach to covalently immobilize an activated oligonucleotide onto the surface of a bead coated with an amine-containing polymer (see columns 6-8) wherein the polymer has a molecular weight from about 600 to about100,000 Daltons (see column 4, last paragraph), Van Ness *et al.*, disclose an immobilized nucleic acid comprising a nucleic acid linked via a covalent bond to a non-nucleotide carrier macromolecule having a molecular weight in excess of 80,000 Daltons (ie., polymer has a molecular weight of

about 100,000 Daltons), which the non-nucleotide carrier macromolecule is directly bound to a solid support (ie., the bead taught by Van Ness *et al.,*) as recited in claim 21.

Regarding claim 22, since Van Ness *et al.*, teach to hybridize a target nucleic acid to an activated oligonucleotide that is covalently attached to a polymer having a molecular weight of about 100,000 Daltons on the surface of a bead (see column 10, last paragraph), Van Ness *et al.*, disclose formulating the immobilized nucleic acid recited in claim 21 as a hybridization probe and introducing the immobilized nucleic acid into a hybridization reaction utilizing the hybridization probe.

Therefore, Van Ness *et al.*, teach all limitations recited in claims 21 and 22.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walker (1995) as applied to claim 1 above, and further in view of Matteucci *et al.*, (US Patent No. 5,434,257, published on July 18, 1995).

The teachings of Walker have been summarized previously, *supra.*

Walker does not disclose that said carrier macromolecule is a homopolyamino acid as recited in claim 3.

Matteucci *et al.*, teach that different kind of compounds such as alkaline phosphatase and polylysine are conjugated to an oligonucleotide (see column 11, third paragraph).

Regarding claims 4-6, since polylysine with a molecular weight in excess of 80,000 Dalton is commercially available at the time the invention was made and it is known that lysine is water soluble and pKa of lysine amino group is 10, Matteucci *et al.*, disclose that the carrier macromolecule (ie., polylysine) in its free state is substantially linear and substantially charged at a pH in the range of 4 to 10 as recited in claim 4, said carrier molecule has a peak molecular weight in the range of in excess of 80,000 to 4,000,000 Daltons as recited in claim 5, and said carrier macromolecule is water soluble as recited in claim 6.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 3 using a primer bound with a carrier macromolecule having a molecular weight in excess of 80,000 Daltons wherein said carrier macromolecule is a homopolyamino acid (ie., polylysine) in view of the patents of Walker and Matteucci *et al.*. One having ordinary skill in the art would have been motivated to do so because Matteucci et al.., have successfully used alkaline phosphatase or polylysine to label a nucleic acid probe and polylysine with a molecular weight in excess of 80,000 Dalton is commercially available at the time the invention was made, and the simple replacement of one well known label with a molecular weight in excess of 80,000 Daltons (ie., alkaline phosphatase) from another well known label with a molecular weight in excess of 80,000 Daltons (i.e., polylysine) during the process for making a primer recited in claim 3 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because both alkaline

phosphatase and polylysine are used as oligonucleotide labels which are exchangeable and the oligonucleotide labeled with polylysine would enhance the binding affinity of the oligonucleotide to its target nucleic acid sequence (see column 11, third paragraph).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. In re Rose 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

11. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Walker (1995) as applied to claim 1 above, and further in view of Westling *et al.,* (US Patnet No. 5,700,921, filed on November 27, 1995).

The teachings of Walker have been summarized previously, *supra.*

Walker does not disclose that said primer is bound to said carrier macromolecule(ie., alkaline phosphatase) via one or more moieties derived from divinyl sulphone as recited in claim 23.

Westling *et al.,* teach that an oligonculeotide is bound to said carrier macromolecule(ie., alkaline phosphatase) via one or more moieties derived from divinyl sulphone (see columns 10 and 11).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art

at the time the invention was made to have performed the methods recited in claim 23 wherein said primer is bound to said carrier macromolecule(ie., alkaline phosphatase) via one or more moieties derived from divinyl sulphone in view of the Patents of Walker and Westling *et al.*. One having ordinary skill in the art would have been motivated to do so because Westling *et al.*, have successfully bound an oligonculeotide to a carrier macromolecule(ie., alkaline phosphatase) via one or more moieties derived from divinyl sulphone, and the simple replacement of one well known method (i.e., the method taught by Walker) from another well known method (i.e., the method taught by Westling *et al.*,) during the process of bonding a primer to a carrier macromolecule(ie., alkaline phosphatase) would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because bonding a primer to a carrier macromolecule taught by Walker and bonding a primer to a carrier macromolecule taught by Westling *et al.*, are functional equivalent methods which are used for the same purpose.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06.

Conclusion

12. Claims 7-12, 14-17, 19, and 20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

13. No claim is allowed.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703)872-9306 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)272-0782.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
June 28, 2004

FRANK LU
PATENT EXAMINER